REMARKS/ARGUMENTS

After entry of this paper, claims 49-50 are pending.

35 USC § 112, First Paragraph Rejection

Claims 49-50 are rejected under this section for the specification assertedly lacking a description of the preparation of 3-(4,4-Dimethyl-2-oxo-1,4-dihydro-2H-benzo[d][1,3]oxazin-6-yl)-5-fluorophenylacetonitrile.

The Examiner specifically asserted the following:

- *There is no matter of making the claimed compound from the disclosure of Example 133;*
- *There is no definitive explanation of what occurs during procedure B;*
- *There is no elucidation in regard to an adequate manner of making the claimed compound from the disclosure of Example 11;*
- *The specification is absent of any adequate preparation steps or explanation directed to making the compound.*

Applicants respectfully request reconsideration and withdrawal of this rejection for the following reasons.

In order for the Examiner to properly reject the claims for lacking written description, the Examiner must provide "...reasonable reasons why a person skilled in the art at the time the application was filed would not have recognized that the inventor was in possession of the invention...".[1] Clearly, it is imperative to establish the knowledge of the skill in the art prior to coming to the conclusion that a specification does not have written description for the claimed subject matter. However, the Examiner noted that "...whether the skilled artisan is apprised of such methods or procedures is of no consequence to the extent that the applicants' have not properly elucidated this particular step in the process of manner of making...".[2] With respect, the Examiner has made an incorrect determination of a lack of written description by not considering the skill in the

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1 MPEP 2163.02, Rev. 6, Sept 2007, page 2100-187

2 Page 2, paragraph 5 of the Office Action dated February 7, 2008

art. The skill in the art for this application would be one with experience in the synthesis, isolation, and characterization of small molecules. Therefore, one with this knowledge would easily be able to prepare the compound of Example 133 using the specification as filed. In fact, the skill in the art required for one to prepare and isolate the compound of Example 133 is much less than the standard for the present application.

With respect, the reaction performed in procedure B of Example 12 is a basic coupling known in the art and provides definitive and detailed information for fulfillment of the written description requirement. Following the coupling step described in procedure B of Example 12, a number of standard purification steps are described regarding the isolation of the desired compound. These standard purification steps include the following:

- Cooling the reaction mixture and quenching using a saturated aqueous ammonium chloride solution;
- Extracting the product using ethyl acetate, which is the most common extraction solvent;
- Rinsing the aqueous layer with more ethyl acetate, which is another standard step performed by those skilled in the art to ensure reduced loss of product;
- Combining the organic layers;
- Washing the organic layers with brine, which is a readily utilized agent utilized to dry the ethyl acetate layer after the aqueous wash;
- Drying the ethyl acetate with $MgSO_4$, which is a common drying agent;
- Removing the ethyl acetate under vacuum; and
- Obtaining the purified product using chromatography.

These purification steps are so basic that one with even an undergraduate degree in chemistry would be able to utilize different reagents, similar in structure to those in Example 12, to prepare the compound of Example 133. Clearly, one of skill in the art would readily understand that variations of procedure B in Example 12 would be necessary in order to isolate and purify the 3-(4,4-Dimethyl-2-oxo-1,4-dihydro-2H-benzo[d][1,3]-oxazin-6-yl)-5-fluoro-phenylacetonitrile product. However, these

variations would readily determined by one with any skill in the art. For example, one would understand the following:

- A slight excess of either starting material would be beneficial, however a 1:1 ratio of starting materials would be sufficient;
- The coupling reaction would not proceed through the F-atom of the benzonitrile noted in Example 133, but would instead proceed through the Br-atom of the benzonitrile;
- A coupling agent, such as $Pd(PPh_3)_4$, must be utilized for the coupling, desirably in a catalytic amount;
- The reaction must be cooled prior to work-up and would then be quenched using an aqueous solution, the reaction would be cooled to room temperature, a variety of aqueous solutions could be utilized for the quench (including saturated aqueous ammonium chloride), and an excess of the aqueous quenching solution would be utilized;
- Extraction of the product would be required and ethyl acetate, which is the most commonly utilized extraction agent, may be utilized, steps would be required for extraction, the necessity to wash the aqueous layers to reduce product loss, and that an excess of the extraction solvent may be utilized;
- Crude product is obtained by removing the solvent from the ethyl acetate extractions using procedures such as vacuum; and
- Purification of the product may be obtained using chromatography and the exact steps and reagents utilized could readily be determined by one skilled in the art.

It is not required that Applicants describe every nuance of the synthetic method of Example 133. It is only necessary to provide one of skill in the art sufficient information, including starting materials and the synthetic methodology, to prepare the compound of Example 133. Therefore, since the skill in the art would more than easily be able to prepare and isolate the compound of Example 133 using the knowledge in the art and teachings of the specification, specifically procedure B of Example 11, the written description standard is fulfilled.

Reconsideration of this rejection is requested.

Double Patenting Rejections

(i) *Claims 49 and 50 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of US Patent No. 6,509,334.*

(ii) *Claims 49 and 50 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of US Patent No. 6,556,358.*

(iii) *Claims 49 and 50 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over the claims of US Patent No. 6,713,478.*

The filing of three (3) Terminal Disclaimers renders the outstanding double patenting rejections moot.

The Director is hereby authorized to charge the fee under 37 CFR § 1.20(d) of $390 for three (3) terminal disclaimers, charge any deficiency in any fees due with the filing of this paper or during the pendency of this application, or credit any overpayment in any fees to our Deposit Account No. 08-3040.

Respectfully submitted,

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